



NOTES

CHILDHOOD PRIMARY BRAIN TUMORS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Most common solid tumor in children < 15 years old
- 20% of all childhood cancer
- Most pediatric brain, spinal cord tumors are primary tumors; originate from central nervous system (CNS) cells
- Most common types
 - Astrocytomas, medulloblastomas, ependymomas, brainstem gliomas
- Better prognosis (generally) than adult brain tumors

RISK FACTORS

- Biologically-male > biologically-female individuals
- Varies with tumor type

COMPLICATIONS

- Dependent on tumor type, location, grade, child's age
- Dependent on size, location, malignant potential of tumor; lesion's mass effect → complications
 - Increased intracranial pressure (ICP) → headache, nausea, vomiting
 - Vision, balance, gait disturbance (common)
 - May be mental changes, normal growth/development disturbance

SIGNS & SYMPTOMS

- May be subtle (slow-onset)/progress quickly
- Headache, nausea/vomiting
 - Morning often worse (waking up)
 - Cough, exercise, body-position change may exacerbate headache
- Mental change
 - Personality/behaviour change, concentration difficulty
- Other associated symptoms
 - Balance/gait disturbance; visual disturbance/loss; hearing/speech difficulty; weakness; numbness

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Head
 - Identify lesion's size, location

LAB RESULTS

Biopsy

- Open surgery/stereotactic biopsy (definitive diagnostic tool)
- Determine type, stage, grade
 - **Grade:** degree of differentiation (tumor cells)
 - **Stage:** extent of spread (tumors cells)

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Lumbar puncture

- Cerebrospinal fluid (CSF) analysis → malignant cell detection

OTHER DIAGNOSTICS

- Visual field examination
 - ↑ ICP → mass effect/swelling → detect central/peripheral vision defects
- Childhood primary brain tumor grades
 - Based on World Health Organization (WHO) grading system (see table)

TREATMENT

- Depends on tumor size/location, child's age
- Goals
 - Eliminate tumor, relieve symptoms, restore brain function

MEDICATIONS

- Chemotherapy
 - Residual tumor/metastasis
- Corticosteroids, diuretics
 - Reduce swelling, alleviate associated ↑ ICP symptoms
- Pain management

SURGERY

- Resection

OTHER INTERVENTIONS

- Radiation
 - Residual tumor/metastasis

W.H.O. TUMOR GRADING SYSTEM

	DESCRIPTION
GRADE I	- Slowly growing - Close to normal appearance - Least malignant - Often associated with good prognosis/long-term survival - Surgery alone may be effective treatment - Examples: pilocytic astrocytoma, craniopharyngioma
GRADE II	- Slowly growing - Slightly abnormal appearance - May spread to nearby tissue - Potential to recur
GRADE III	- Malignant, reproducing abnormal cells - Often grow into nearby structures - Tend to recur
GRADE IV	- Most malignant - Rapidly reproduce, lesion's centre often necrotic - Abnormal cell appearance - Example: glioblastoma multiforme

CRANIOPHARYNGIOMA

osms.it/craniopharyngioma

PATHOLOGY & CAUSES

- Rare benign non-glial epithelial CNS tumor
 - Often within sellar/suprasellar space
- Hypothesis
 - Derived from Rathke's cleft/squamous cell crests along craniopharyngeal duct
- Gross pathology
 - Cholesterol crystals in "motor oil"-like fluid within tumor, homogeneous

TYPES

- Adamantinomatous
 - Primarily children, often single/multiple cysts
- Papillary
 - Adults (almost exclusively), solid lesions

RISK FACTORS

- Bimodal age distribution
 - 5–14 years old (children), 50–70 years old (adults)

COMPLICATIONS

- Hypopituitarism, hydrocephalus, ↑ ICP

SIGNS & SYMPTOMS

- Headache, nausea, vomiting
- Visual disturbance/loss (i.e. **bitemporal hemianopia**)
- Endocrine abnormality
 - Affects growth, thyroid/adrenal function, diabetes insipidus
- Behavioral change (ie. hypersomnia)

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Mass visualization
- Other common findings
 - Suprasellar region **calcification**, one/more supra/parasellar region cysts

Histopathology

- Cysts with stratified squamous epithelium, cholesterol crystals, keratin pearls

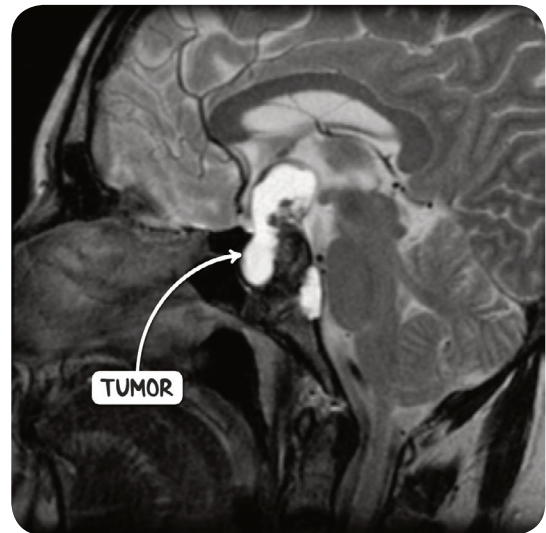


Figure 67.1 An MRI scan of the head in the sagittal plane demonstrating a craniopharyngioma, adamantinomatous subtype. The tumor has clear solid and cystic components with abundant calcification.

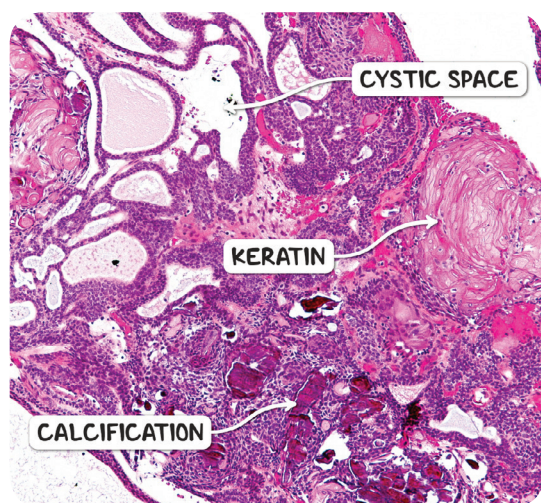


Figure 67.2 A histological section of a craniopharyngioma, adamantinomatous type. The tumor is composed of cystic spaces, calcifications and keratin.

TREATMENT

MEDICATIONS

- Endocrine replacement therapy: specific endocrine deficiency-dependent

SURGERY

- Resection

OTHER INTERVENTIONS

- Radiotherapy

EPENDYMOMA

osms.it/ependymoma

PATHOLOGY & CAUSES

- Uncommon glial tumor
 - Arises from ependymal cells lining ventricular system, spinal cord's center
- Located intracranially (children), within spinal canal (adults)
- Often form ependymal pseudorosettes
 - Tumor cells arranged around vessels, fibrils pointing towards vessel

TYPES

- Five subtypes: WHO grade classification
 - Subependymoma: grade I
 - Myxopapillary ependymoma: grade I
 - Ependymoma: grade II
 - RELA fusion-positive ependymoma: grade II/grade III (with RELA gene change)
 - Anaplastic ependymoma: grade III

RISK FACTORS

- Neurofibromatosis type II (NF2)-diagnosed individuals (more common)

COMPLICATIONS

- Fourth ventricle blockage → hydrocephalus → headache, nausea, vomiting
- Tumor mass effect

SIGNS & SYMPTOMS

- Headache, visual disturbance/loss, nausea, vomiting, ataxia (gait, balance disturbance), vertigo, papilledema, cranial-nerve palsy, seizure/focal neurologic deficit, back pain, limb numbness/weakness

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Hyperdense with enhancement, commonly see cysts, calcifications

MRI

- Hypointense lesion, extension into Luschka foramen may be seen

LAB RESULTS

Histological examination

- Cells with round/oval nuclei, dense fibrils forming canal structure
- **Perivascular pseudorosettes**
 - Cells arranged around vessels with thin ependymal processes directed inwards
- Immunohistochemical markers include glial fibrillary acid protein, epithelial membrane antigen

CSF cytology

- Guides tumor staging

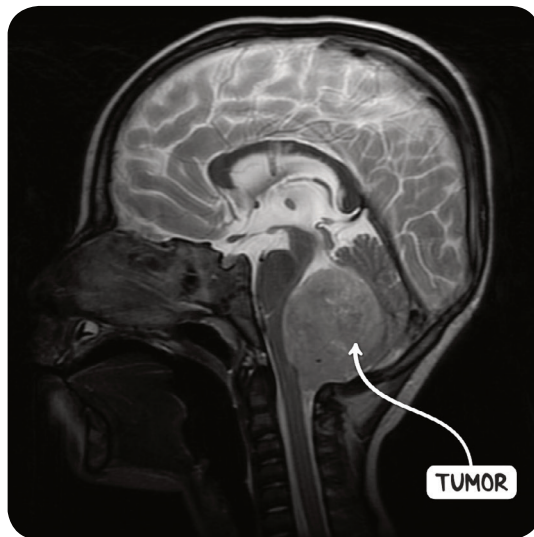


Figure 67.4 An MRI scan of the head of a child demonstrating an ependymoma in the posterior fossa, compressing the cerebellum.

TREATMENT

MEDICATIONS

- Chemotherapy

SURGERY

- Resection

OTHER INTERVENTIONS

- Adjuvant radiotherapy

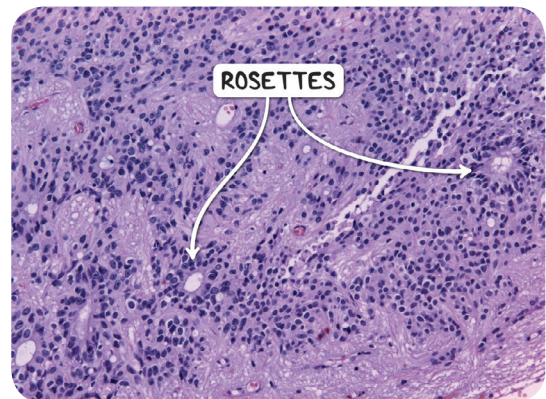


Figure 67.3 The histological appearance of an ependymoma. The tumor is composed of monomorphic cells which form ependymal rosettes, with a central clearing.

MEDULLOBLASTOMA

osms.it/medulloblastoma

PATHOLOGY & CAUSES

- Most common pediatric malignant primary brain tumor
 - Arises from cerebellum's primitive neuroepithelial cells
- Usually forms midline mass along roof of fourth ventricle (between brainstem/cerebellum)
- WHO grade IV classification

TYPES

- Categorized as desmoplastic, classic, large-cell, anaplastic, variants
- Gene expression profiling recognizes four molecular subgroups

Wingless (WNT)

- Excellent prognosis
- 1:1 biologically male/biologically female ratio
- 10–12 years old (peak incidence)
- Classic histology (majority)
- Often CTNNB1 gene (encodes beta-catenin) mutation

Sonic Hedgehog (SHH)

- Intermediate prognosis
- 1:1 biologically male/biologically female ratio
- Infants < four years old, adults > 16 years old
- Classic, large-cell, anaplastic, desmoplastic, with extensive nodularity

Group 3

- Poor prognosis
- 2:1 biologically male/biologically female ratio
- 4–16 years old
- Classic/large-cell anaplastic histology, associated with Myc amplification, poorly-defined lesions (better contrast enhancement than group 4 lesions)

Group 4

- Poor prognosis
- 2:1 biologically male/biologically female ratio
- 4–16 years old
- Classic histology, well-defined lesions (limited contrast enhancement)

RISK FACTORS

- 2:1 biologically male/biologically female ratio
- 3–8 years old
- Certain inherited familial syndromes
 - Ataxia-telangiectasia, Rubinstein-Taybi syndrome, Gorlin syndrome, Turcot's syndrome, Li-Fraumeni syndrome

COMPLICATIONS

- Frequent metastasis → other brain, spinal cord parts
- Fourth ventricle blockage → hydrocephalus → headache, nausea, vomiting
- Tumor's mass effect

SIGNS & SYMPTOMS

- Headache; nausea; vomiting; ataxia (gait/balance disturbance), falls; diplopia; papilledema; positional dizziness, nystagmus; bulging anterior fontanelle; visual disturbance/loss

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Often appear as vermis mass → fourth ventricle effacement → obstructive hydrocephalus
- Hyperdense, +/- cysts, +/- calcifications

MRI

- Heterogeneous mass; calcification, necrosis, cyst formation
- May see surrounding edema

LAB RESULTS

Histological examination

- Variable cellular atypia
- **Homer Wright rosette**; dark tumor cells spherically arranged around pale eosinophilic neurofibrils
- INI1-positive (tumor suppressor gene marker)

Lumbar puncture

- CSF analysis
 - Malignant cell detection

TREATMENT

MEDICATIONS

- Chemotherapy

SURGERY

- Tumor resection

OTHER INTERVENTIONS

- Radiotherapy

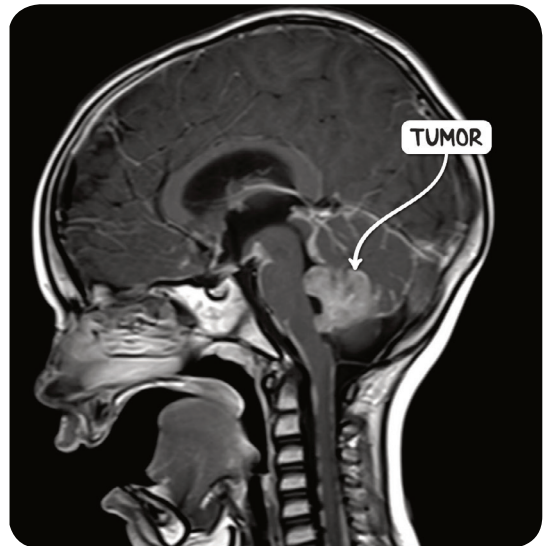


Figure 67.5 An MRI scan of a child in the sagittal plane demonstrating a medulloblastoma. In childhood, they commonly arise in the posterior fossa at the roof of the fourth ventricle.



Figure 67.6 A medulloblastoma forming Homer-Wright rosettes, with no central clearing.

PILOCYTIC ASTROCYTOMA

osms.it/pilocytic-astrocytoma

PATHOLOGY & CAUSES

- Primary tumor
 - Arises from astrocytes
 - AKA juvenile pilocytic astrocytoma/ cystic cerebellar astrocytoma
- Mainly occurs in children (majority 0–30 years old)
- Often arises in cerebellum, hypothalamic region, along optic pathway
- Tumors slow growing, benign (WHO grade I)
- Associated with cyst formation, often well-circumscribed
- Strong neurofibromatosis type I (NF-1) association
- Microscopic appearance
 - Elongated hair-like projections, Rosenthal fibers (characteristic feature)

SIGNS & SYMPTOMS

- Altered mental status; headache, nausea, vomiting; gait disturbance, ataxia; weakness; seizure; visual disturbance, nystagmus, papilloedema; aphasia/ dysphasia

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Lesion (hypodense), calcification/ hemorrhage area (hyperdense)

MRI (head)

- Range of appearances
 - Cystic component(s) with mural nodule (enhancing, nonenhancing cyst wall); heterogeneous, mixed solid; homogeneous solid

- Spectroscopy/perfusion MRI head
 - Determines tumor grade

LAB RESULTS

Biopsy

- Mass
 - Heterogeneous/homogeneous/mixed; cystic; solid; with/without hemorrhage, necrosis

OTHER DIAGNOSTICS

- Ophthalmological evaluation/visual field testing
 - May detect visual field deficit

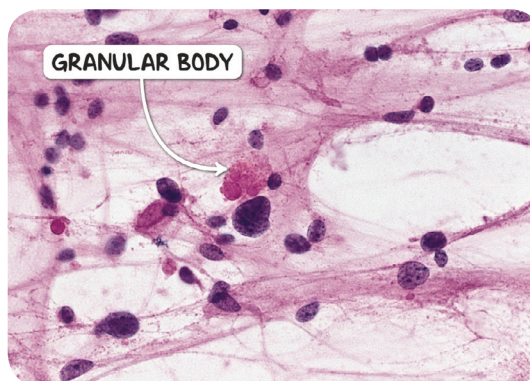


Figure 67.7 A brain biopsy smear from a pilocytic astrocytoma demonstrating malignant astrocytes with pleomorphic, hyperchromatic nuclei. In addition there is an eosinophilic granular body, commonly seen in such tumors.

TREATMENT

MEDICATIONS

- Chemotherapy

SURGERY

- Resection (location often prohibits total resection)

OTHER INTERVENTIONS

- Radiotherapy
- Observation (when asymptomatic)

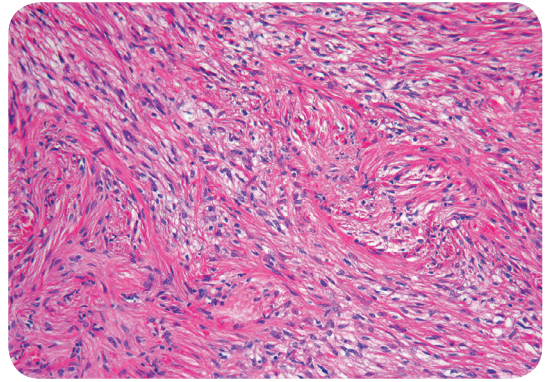


Figure 67.8 The histological appearance of a pilocytic astrocytoma. There are bipolar neoplastic cells arranged in fascicles with elongated hair-like processes.

PINEALOMA

osms.it/pinealoma

PATHOLOGY & CAUSES

- Rare tumor that arises from cells in the pineal region
- May result in endocrine disruption, obstructive hydrocephalus, and compression of adjacent structures (cerebellum, brainstem)
- Occurs any age; malignancy more common in children (< eight years old)

TYPES

- Four pinealoma types
 - Germ cell tumors
 - Papillary tumors
 - Pineal parenchymal cell tumors
 - Glial cell tumors
- Other miscellaneous tumors and cysts in the pineal region

RISK FACTORS

- RB1 gene inheritance
- Previous radiation exposure

COMPLICATIONS

- Precocious puberty
 - Homeostatic hypothalamic-pituitary axis disruption → puberty onset in biologically-male individuals (< nine years old), biologically-female individuals (< eight years old)
 - ↓ melatonin production (may result) → impaired circadian rhythm regulation
- Physical ventricular system obstruction → ↑ ICP → hydrocephalus

SIGNS & SYMPTOMS

- Parinaud's syndrome (upward gaze paralysis, pupillary areflexia), pseudo-Argyll Robertson pupils, convergence-retraction nystagmus, eyelid reaction (Collier's sign)
- Headache; nausea; vomiting; visual, balance, gait disturbance; fatigue/irritability; insomnia

DIAGNOSIS

DIAGNOSTIC IMAGING

Head CT scan/MRI

- May appear cystic/partially cystic
- Often lobulated, seen as heterogeneous mass
- Usually 2.5–4 cm/1–1.6in wide, well circumscribed in pineal region; contrast-enhanced rim in cystic forms

LAB RESULTS

- Hormonal evaluation
 - Melatonin (indicates pineal gland pathology)
- Lumbar puncture
 - CSF analysis for detection of malignant cells
 - α -fetoprotein/ β -HCG tumor markers indicate germinal origin
- Biopsy
 - Determines type, stage; open surgery/ stereotactic biopsy

OTHER DIAGNOSTICS

- Visual field examination
 - **Defect detection:** central, peripheral vision; swelling around optic nerve ($\uparrow$ ICP sign)

TREATMENT

SURGERY

- Resection +/- shunt (drain excess CSF)

OTHER INTERVENTIONS

- Adjuvant radiotherapy (malignant tumors)